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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/618,178 | 07/11/2003 | Daniel J. Burdick | P1862R1C1 | 4372 |

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| EXAMINER | |
|---|---|
| AULAKH, CHARANJIT | |
| **ART UNIT** | **PAPER NUMBER** |
| 1625 | |

DATE MAILED: 04/15/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/618,178 | BURDICK ET AL. | |
| | Examiner | Art Unit | |
| | Charanjit S. Aulakh | 1625 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) 1-23 is/are pending in the application.

4a) Of the above claim(s) 6-8 is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-5 and 9-23 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 1.
4) ☒ Interview Summary (PTO-413) Paper No(s)/Mail Date. 04/09/04 .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

1. Claims 1-23 are pending in the application.

### *Election/Restrictions*

2. Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-5 and 9-23, drawn to compounds of formula (I) where CY represents a non-aromatic heterocycle, X represents –CH2-NR6-divalent hydrocarbon chain ( not interrupted with N, O, S, SO or SO2 ) and L represents a divalent hydrocarbon chain ( not interrupted with N, O, S, SO, SO2 or an amino acid residue ), pharmaceutical compositions containing these compounds and a method of using these compounds, classified in class 546, subclass 225.

II. Claims 1-23, drawn to compounds of formula (I) other than defined above for group I, pharmaceutical compositions containing these compounds and a method of using these compounds, classified in class 548, subclass 537.

3. The inventions I and II as defined above are patentably distinct, each from the other since they are structurally so divergent that a reference showing compounds of invention I would not render compounds of invention II prima facia obvious. Search required for e.g ; compounds of invention I in class 546 is not the same search required for e.g ; compounds of invention II in class 548 and therefore, constitutes a burdensome search.

4. During a telephone conversation with the applicant's attorney, Mr. David W. Evans on April 9, 2004, a provisional election was made with traverse to prosecute the invention

of group I, claims 1-5 and 9-23. Affirmation of this election must be made by applicant in replying to this Office action. Claims 6-8 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention. It is of note that group II is subject to further restriction based on the values of variables L, X and CY in the future applications.

5. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

***Claim Rejections - 35 USC § 112***

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 21-23 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The following eight different factors (see Ex parte Foreman, 230 USPQ at 547; Wands, In re, 858. F. 2d 731, 8 USPQ 2d 1400, Fed. Cir. 1988) must be considered in order for the specification to be enabling for what is being claimed :

Quantity of experimentation necessary, the amount of direction or guidance provided, presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability and the breadth of claims. In the instant case, the specification is not enabling based on atleast four of the above mentioned eight factors such as quantity of experimentation necessary, the amount of direction or guidance provided, presence of working examples, the state of the prior art and the breadth of claims.

The instant compounds are LFA-1 antagonists based on in vitro data as demonstrated in example 11 and table 1. It is well known in the art that in vitro activity of a compound does not necessarily correlate with their in vivo activity since in vivo activity is influenced by various factors such as absorption, metabolism etc. There is no teaching either in the specification or prior art showing diseases or conditions which are mediated by LFA-1. There is no teaching or guidance in the specification that how the instant compounds having inhibitory activity at LFA-1 in vitro will treat disease conditions following their in vivo administration. There is no teaching, guidance or presence of working examples to show the effectiveness of the instant compounds in known animal models of any disease condition including inflammatory diseases following their in vivo administration. LFA-1 may be one of the several other known mechanisms responsible for the etiology of any inflammatory disease condition and therefore, the instant compounds may have utility in treating but not inhibiting or preventing that specific disease condition. The instant compounds of formula (I) encompasses hundreds of thousands of compounds based on variables R1-R5, X, L, Y and Cy and therefore, in

absence of such teachings, guidance or presence of working examples, it would require undue experimentation to demonstrate the effectiveness of instant compounds in known animal models of disease conditions where etiology of LFA-1 is implicated and hence their utility.

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 1-5 and 9-23 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In independent claim 1, the value of variables CY, Y and R1 defined as –heterocycle – is indefinite since the size of the ring, the number and types of heteroatoms present in the ring are not defined.

In independent claim 1, the values of variables X and L defined as –a divalent hydrocarbon chain--- is indefinite since the length of the chain and degree of saturation ( alkyl, alkenyl, alkynyl etc. ) is not defined.

In claim 1, last three lines, the applicants have put a proviso that X is other than cyclohexyl. However, according to definition of variable X, it can not be cyclohexyl. An appropriate correction is required.

In claim 21, it is not clear whether this method is directed to in vitro method or in vivo method? What is meant by protein ligand? Is it plasma, blood, specific tissue cell ? What is the end result by inhibiting binding of LFA-1 ? Does it help in treating some

specific disease condition? If so, the applicants are suggested to include the specific disease condition in the claim.

In claim 22, it is not clear what are the diseases or conditions which are mediated by LFA-1 in a mammal? Also, is it overactivity or underactivity of LFA-1 which is responsible for the etiology of specific disease or condition?

In claim 23, the term ---inflammatory disease or condition--- is indefinite since specific disease or condition is not defined. Also, the term –inhibiting – is indefinite since the degree of inhibition ( 20%, 40%, 60% or 100% ) is not defined and furthermore, it is not clear whether the compound is being administered to a mammal which is normal, prone to inflammatory disease or to a mammal having inflammatory disease.

10. There are two claims numbered 23. An appropriate correction is required.

11. Claims 1-5 and 9-23 are objected as containing non-elected subject matter.

***Allowable Subject Matter***

12. The following is a statement of reasons for the indication of allowable subject matter: The instant compounds directed to the elected subject matter are allowable over the prior art since they are neither disclosed nor obvious over the prior art. In the prior art, Genetech, Inc.( WO 99/49856, cited on applicants form 1449 ) discloses antagonists for treatment of CD11/CD18 adhesion receptor mediated disorders which are closely related to instant compounds. However, the closely related compounds ( see last two compounds at bottom of page 46 ) differ from the instant compounds in having an aromatic heterocycle instead of non-aromatic heterocycle for variable Cy and

furthermore, there is no teaching, suggestion or motivation in the prior art to modify the compounds of Genetech, Inc. to prepare the instant compounds.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Charanjit S. Aulakh whose telephone number is (571)272-0678. The examiner can normally be reached on Monday through Friday, 8:30 A.M. to 5:00 P.M..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph McKane can be reached on (571)272-0699. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

C. S. Aulakh

Charanjit S. Aulakh
Primary Examiner
Art Unit 1625